

GenCore version 4.5
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OM protein - protein search, using sw model

Run on: September 27, 2001, 16:41:22 ; Search time 34.59 Seconds
(without alignments)
571.362 Million cell updates/sec

Title: US-09-483-543a-9

Perfect score: 1733

Sequence: 1 KRGCAGNDFSESRSSWTWGR.....SGCGXGLEVLRFQGPVRKXG 326

Scoring table:
BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 412676 seqs, 60623988 residues

Total number of hits satisfying chosen parameters: 412676

Minimum DB seq length: 0
Maximum DB seq length: 200000000
Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database :

- 1: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1980.DAT.*
- 2: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1981.DAT.*
- 3: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1982.DAT.*
- 4: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1983.DAT.*
- 5: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1984.DAT.*
- 6: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1985.DAT.*
- 7: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1986.DAT.*
- 8: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1987.DAT.*
- 9: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1988.DAT.*
- 10: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1989.DAT.*
- 11: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1990.DAT.*
- 12: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1991.DAT.*
- 13: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1992.DAT.*
- 14: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1993.DAT.*
- 15: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1994.DAT.*
- 16: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1995.DAT.*
- 17: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1996.DAT.*
- 18: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1997.DAT.*
- 19: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1998.DAT.*
- 20: /SIDSR8/gcgcdata/geneseq/geneseqp/AA1999.DAT.*
- 21: /SIDSR8/gcgcdata/geneseq/geneseqp/AA2000.DAT.*
- 22: /SIDSR8/gcgcdata/geneseq/geneseqp/AA2001.DAT.*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	1605	92.6	304	17	AAW05409
2	1129	65.1	256	16	AAAR85919
3	917.5	52.9	303	19	AAW42071
4	913.5	52.7	303	17	AAAR7439
5	321	18.5	79	19	AAW54313
6	257	14.8	50	21	AAAB12071
7	257	14.8	217	18	AAW18063
8	224	12.9	217	16	AAAR85918
9	224	12.9	217	18	AAW14004
10	224	12.9	217	19	AAW42070
11	222	12.8	217	16	AAAR84636

12	210	12.1	317	13	AAAR26061
13	177	10.2	1290	17	AAAR90589
14	174	10.0	845	21	AAAY49419
15	172.5	10.0	797	20	AAAY27125
16	167	9.6	844	13	AAAR25671
17	159.5	9.2	287	20	AAAY22236
18	159.5	9.2	847	20	AAAY22237
19	158.5	9.1	330	21	AAAY97991
20	158	9.1	1215	20	AAAY32156
21	158	9.1	1220	20	AAAY32155
22	157	9.1	462	17	AAW05395
23	157	9.1	509	17	AAW05399
24	157	9.1	641	20	AAAY32158
25	157	9.1	1144	20	AAAY32154
26	156.5	9.0	330	21	AAAY69388
27	154.5	8.9	1715	21	AAAY57449
28	152	8.8	1214	21	AAAY57444
29	151.5	8.7	320	19	AAW76830
30	149	8.6	464	18	AAW26496
31	149	8.6	464	18	AAW25116
32	149	8.6	464	20	AAW80420
33	149	8.6	464	22	AAAB6391
34	147.5	8.5	788	17	AAW05393
35	147	8.5	1197	21	AAAY57445
36	147	8.5	1658	15	AAAR6685
37	144.5	8.3	1047	11	AAAR6328
38	144.5	8.3	1047	12	AAAR1137
39	144.5	8.3	1047	13	AAAR2536
40	144.5	8.3	870	15	AAAR5924
41	143.5	8.3	870	15	AAAR5924
42	141.5	8.2	1683	21	AAAY71160
43	141	8.1	553	18	AAW26495
44	141	8.1	553	18	AAW25115
45	141	8.1	553	20	AAW80419

ALIGNMENTS

RESULT 1	
ID	AAW05409 standard; Protein; 304 AA.
AC	
XX	AAW05409;
DT	23-FEB-1998 (first entry)
AC	
XX	
DE	Mouse Crk protein.
XX	
KW	Src-homology region 3 domain; human; mouse; SH3 domain; cell growth;
KW	cellular signaling element; cellular structural element; malignancy;
KW	protein identification; functional domain; protein screening;
KW	cellular signal transduction process.
XX	
OS	Mus musculus.
XX	
FH	Key
FT	Misc-difference 167 Location/Qualifiers
FT	Misc-difference 168 /note= "encoded by GAG"
FT	Misc-difference 168 /note= "encoded by GAG"
XX	
PN	W09631625-A1.
PD	10-OCT-1996.
XX	
PP	04-APR-1996; 96WO-US04454.
XX	
PR	03-APR-1996; 96US-0630915.
PR	07-APR-1995; 95US-0417872.
XX	
PA	(CYTO-) CYTOGEN CORP.
PA	(UYNC-) UNIV NORTH CAROLINA.

Growth Factor Rece
Phospholipase C-ga
PKA substrate, Vav
Amino acid sequenc
Mouse vav proto on
Human KDR signal t
Human KDR signal t
Human Grf40, a sig
Human SH3D1A prote
Human SH3D1A prote
Human SH3P17 prote
Human clone 65 pro
Human SH3D1A prote
Human SH3D1A prote
Amino acid sequenc
Mouse Eesl, protei
Mouse Eesl, protei
Human Eesl protein
Human GRP protein
CD2-associated int
CD2-associated int
CD2-associated int
Human CD2 associat
Mouse SH3P12 prote
Mouse Eesl protein
Mouse Eesl, protei
Peptide P9 inhibit
Sequence of full l
GAP6 encoded by 1a
Lambda clone 101 p
Human GAP protein.
Rat phosphodiester
CD2-associated int
CD2-associated int
CD2-associated int

XX Fowlkes DM, Hoffman N, Kay BK, McConnell SJ, Sparks AB;
 XX WPI: 1996-465045/46.
 DR N-PSDB: AAT93808.
 XX
 PT Identifying polypeptide(s) having specific functional domain (esp.
 PT SH3 domain) - comprises detecting selective binding to recognition
 PT unit, regardless of sequence homology
 XX
 PS Claim 102; Fig 41; 174pp; English.
 XX
 CC AAM05405-W05411 represent human and mouse Src-homology region 3 (SH3)
 CC domain containing proteins that can be used in the method of the
 CC invention. SH3 domain containing proteins play a role in signalling and
 CC structural elements of cells. The method of the invention is for
 CC identifying polypeptides containing functional domains of interest
 CC (especially SH3 domains). The method comprises contacting a multivalent
 CC recognition unit (RU) complex with a number of peptides and identifying
 CC polypeptides having a selective binding affinity for the RU complex. The
 CC method is based on functional similarities and does not rely on sequence
 CC similarities. Prior methods only gave limited success for identifying
 CC proteins which contain an SH3 domain due to the minimal sequence
 CC homology among known SH3 proteins. It has been found that small peptide
 CC RUs in multivalent form have reduced specificity for a given functional
 CC domain compared to monomer RUs. Multivalent RU complexes are particularly
 CC suited to screening for polypeptides containing functional domains that
 CC are similar to, but not identical in sequence to, the original target
 CC functional domain. The new method enables proteins having a common
 CC function to be identified. Identification of novel SH3 proteins will be
 CC useful for a better understanding of cell growth, malignancy, signal
 CC transduction processes, etc. New candidate drugs can be identified, and
 CC their specificities (e.g. pharmacological activities) can be assessed
 CC using the method of the invention.
 XX
 XX Sequence 304 AA:
 SQ
 Query Match 92.6%; Score 1605; DB 17; Length 304;
 Best Local Similarity 99.7%; Pred. No. 2.1e-134;
 Matches 302; Conservative 0; Mismatches 1; Indels 0; Gaps 0;
 QY 5 AGNFDSEERSWVGRSLRQEAVALLOGRHGFLVRDSTSPGDYVLSVSENSRVSHYI 64
 DB 2 agndfseerswvgrslrqeavalllqgrhgvflvrdsstspgdyvlsvsensrvshyl 61
 QY 65 INSSGPRPVPSPAPQPPGVPSPSLRITGQDFDLSPLALFEYKIRHYDITTLTLEPVARS 124
 DB 62 insgprpvpvspapqpvpvsprritgndqfidslpallefykhyldttcltlepvars 121
 QY 125 ROGSGVILROEAEYVRALFDNGNDEEDLPFRKGDILIRIRDKPEEQMNAEDSEGRGM 184
 DB 122 rggsgvillrgeaeeyvralfdngndeedlpfrkkgdillirirdkpeeqmnaedsegrgkm 181
 QY 185 IPVPYVEKYRPASASVSALLIGNQEGSHPOP LGPEPGPAPQPSVNTPLPNLONGPPIYAR 244
 DB 182 ipvyveykyrpasasvsallignqegshpoplgpepgpapsvntplpnlngpbiyar 241
 QY 245 VIOGRVNAVDTKRLALEVGEVYKTKINSGWEGECNKRGHFPPTTHVRLDDOONPDE 304
 DB 242 vigrvnavdtkrlalevgeyvktkinsgwegecnkrghfpptthvrllddognpde 301
 QY 305 DFS 307
 DB 302 dfs 304

DT 16-MAY-1996 (first entry)
 XX
 DE Human GRB-3.
 XX
 KW GRB-3; growth factor receptor bound; tyrosine kinase; regulation;
 KW cell growth; cellular metabolism; screening; signal transduction;
 KW cancer; diabetes; CORF technique; cloning of receptor targets.
 XX
 OS Homo sapiens.
 XX
 PN WO9524426-A1.
 XX
 PD 14-SEP-1995.
 XX
 PF 13-MAR-1995; 95WO-US03385.
 XX
 PR 11-MAR-1994; 94US-0208887.
 XX
 PA (UYNV) UNITV NEW YORK STATE.
 XX
 PI Margolis BL, Schlessinger J, Skolnik EY;
 XX
 DR WPI: 1995-328235/42.
 DR N-PSDB: AAT07168.
 XX
 PT DNA encoding tyrosine kinase-binding proteins - used to screen
 PT agents capable of modulating cell growth or cellular metabolism
 XX
 PS Disclosure; Fig 34A-C; 215pp; English.
 XX
 CC Using a new cloning technique, CORF (cloning of receptor targets)
 CC several new tyrosine kinase (TK) binding proteins were isolated. Growth
 CC factor receptor bound proteins GRB-1, GRB-2, GRB-3, GRB-4, GRB-7 and
 CC GRB-10 were isolated using this method. This sequence represents GRB-3.
 CC The proteins bind to a tyrosine-phosphorylated domain of a eukaryotic
 CC TK. GRB proteins can be used for screening agents which are capable
 CC of modulating cell growth that occurs via signal transduction through
 CC TKs. Such agents can be used to prevent or inhibit cell growth or to
 CC counteract tumour development. GRB proteins are also useful for
 CC identifying susceptibility to diseases associated with alterations in
 CC cellular metabolism mediated by TK pathways e.g. cancer and diabetes.
 XX
 XX Sequence 256 AA:
 SQ
 Query Match 65.1%; Score 1129; DB 16; Length 256;
 Best Local Similarity 98.2%; Pred. No. 2.7e-92;
 Matches 215; Conservative 0; Mismatches 4; Indels 0; Gaps 0;
 QY 5 AGNFDSEERSWVGRSLRQEAVALLOGRHGFLVRDSTSPGDYVLSVSENSRVSHYI 64
 DB 33 agndfseerswvgrslrqeavalllqgrdgvflvrdsstspgdyvlsvsensrvshyl 92
 QY 65 INSSGPRPVPSPAPQPPGVPSPSLRITGQDFDLSPLALFEYKIRHYDITTLTLEPVARS 124
 DB 93 insgprpvpvspapqpvpvsprritgndqfidslpallefykhyldttcltlepvars 152
 QY 125 ROGSGVILROEAEYVRALFDNGNDEEDLPFRKGDILIRIRDKPEEQMNAEDSEGRGM 184
 DB 153 rggsgvillrgeaeeyvralfdngndeedlpfrkkgdillirirdkpeeqmnaedsegrgkm 212
 QY 185 IPVPYVEKYRPASASVSALLIGNQEGSHPOP LGPEPGP 223
 DB 213 ipvyveykyrpasasvsallignqegshpoplgpepgp 251

RESULT 2
 AAR85919
 ID AAR85919 standard; Protein; 256 AA.
 XX
 AC AAR85919;
 XX

RESULT 3
 AAM42071
 ID AAM42071 standard; Protein; 303 AA.
 XX
 AC AAM42071;
 XX
 DT 04-JUN-1998 (first entry)

```

XX  Human Crk-like protein CrkL.
DE  Crk-like; CrkL; CML; translation initiation site; bcr-abl;
XX  chronic myelogenous leukaemia; cancer.
XX  Homo sapiens.
XX  Key
FH  Location/Qualifiers
FT  14..64
FT  Domain /label= SH2
FT  78..101
FT  Domain /label= SH2'
FT  131..179
FT  Domain /label= SH3
FT  238..290
FT  Domain /label= SH3
FT  /note="this domain is designated SH4 in the disclosure"
XX  MO9801547-A1.
XX  15-JAN-1998.
XX  PD
XX  PF 08-JUL-1997; 97WO-US10101.
XX  PR 08-JUL-1996; 96US-0679437.
XX  XX
XX  (TEXTA ) UNIV TEXAS SYSTEM.
XX  PI Arlinghaus RB, Lopez-Berestein G, Tari AM;
XX  DR WPI: 1998-110229/10.
XX  DR N-PSDB; AAV09214.
XX  PT Use of anti-sense oligo:nucleotide(s) to Grb2 or CrkL nucleic acids
XX  PT - for inhibiting growth of cancer cells in treatment of cancers,
XX  PT particularly chronic myelogenous leukaemia
XX  PS Disclosure; Fig 5; 47pp; English.
XX  CC This is the sequence of human CrkL. Translation of CrkL cDNA can be
XX  CC inhibited by oligonucleotides of specific composition that
XX  CC hybridise to its translation initiation site. The oligonucleotide
XX  CC compositions can be used for treating, particularly chronic
XX  CC myelogenous leukaemia (CML). See AAV09216.
XX  SO Sequence 303 AA;

Query Match 52.9%; Score 917.5; DB 19; Length 303;
Best Local Similarity 56.6%; Pred. No. 1.9e-73;
Matches 185; Conservative 33; Mismatches 56; Indels 53; Gaps 6;

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```

OY 279 EGECNGKRGHFFPTHYRLDDQNPDED 305
DB 276 egevgngrgkglfptfhvkifdpqnden 302

RESULT 4
AAR77439
ID AAR77439 standard; Protein; 303 AA.
XX
XX AAR77439;
XX
XX 21-JUL-1996 (first entry)
XX
XX Mouse CRKL protein.
XX
XX Mouse CRKL protein; tyrosine phosphorylation; diagnosis;
XX chronic myelogenous leukaemia; acute lymphoblastic leukaemia;
XX Philadelphia chromosome; BCL; ABL; treatment.
XX
XX Mus musculus.
XX
XX Key
FH Binding-site Location/Qualifiers
FT Domain 9..103
FT Domain /note="SH2 domain"
FT Domain 131..179
FT Domain /note="N-terminal SH3 domain"
FT Modified-site 193..210
FT Domain /note="tyrosine phosphorylation site"
FT 238..290
FT Domain /note="C-terminal SH3 domain"
XX
XX MO9531545-AZ.
XX
XX 23-NOV-1995.
XX
XX 12-MAY-1995; 95WO-US05957.
XX
XX 13-MAY-1994; 94US-0242513.
XX
XX (CHIL-) CHILDRENS HOSPITAL LOS ANGELES.
XX
XX Groffen JH, Heisterkamp NC, Ten Hoeve J;
XX
XX WPI: 1996-010931/01.
XX
XX N-PSDB; AAT04144.
XX
XX Diagnosis of tyrosine phosphorylated CRKL protein cancers - by
XX detecting increased level of CRKL protein or CRKL binding protein,
XX also compms. for treating chronic myelogenous leukaemia.
XX
XX Claim 37; Fig 10b; 74pp; English.
XX
XX The mouse CRKL protein may be used in the diagnosis of Philadelphia
XX chromosome-positive leukemias. For example, since CRKL is clearly
XX tyrosine-phosphorylated in chronic myelogenous leukaemia and
XX Philadelphia chromosome (Ph)-positive acute lymphoblastic leukaemia
XX patients expressing the BCR/ABL protein, but not in BCR-ABL-negative
XX peripheral blood cells, tyrosine phosphorylation of CRKL may be used
XX as a diagnostic indicator for BCL/ABL activity in Ph-positive
XX leukaemia. Thus, overexpression of tyrosine-phosphorylated CRKL
XX protein, or an increase in protein, gene copy number or mRNA is
XX indicative of Ph-positive leukaemia. Fragments of the CRKL protein
XX may also be used in the treatment of individuals with cancers
XX arising from cells which express the CRKL protein by inhibition of
XX the synthesis or activity of the CRKL protein.
XX
XX Sequence 303 AA;

Query Match 52.7%; Score 913.5; DB 17; Length 303;
Best Local Similarity 56.0%; Pred. No. 4.4e-73;
Matches 183; Conservative 35; Mismatches 56; Indels 53; Gaps 6;

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Query Match 12.9%; Score 224; DB 16; Length 217;

Best Local Similarity 27.9%; Pred. No. 4e-12;

Matches 53; Conservative 44; Mismatches 57; Indels 36; Gaps 7;

```

QY 7 NFDSEERSWYGRSLRQDAVALLOGQRH-GVFLVRDSTSPGDVYLSVSENSRSHYIT 65
   | : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
   | : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
Db 51 nylemkhpwffgkikprakeemlskgrhdgafliresepdpdflsvkfgndvqhfv 110
   | : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
QY 66 NSSGPRPPVPPAPQPPVSPSRLRIGDQFDSLPALLEFYKIHVLDPTTLIEPVARSR 125
   | : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
Db 111 lrdg-----agkyflwvkvkfnslnelvqyhr-----sts-----vsrnq 144
   | : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
QY 126 QSGSVILRQ-----EEAEYRALFDFENGNDIEDLPFKKGILIRIDKPEQGMNAEDSEG 180
   | : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
Db 145 q---lftrdieqvppqplvqalfdldpqedgelfgrgdfihvmdnsdpnwkg-a-chg 200
   | : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
QY 181 KRGMIPVPV 190
   | : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
Db 201 qtgmfprrny 210

```

RESULT 9

AAW14004
ID AAW14004 standard; Protein; 217 AA.

AC AAW14004;

DT 24-JUN-1997 (first entry)

DE Human GRB2.

OS SH2-containing inositol phosphatase; SHIP.

KM Inositol polyphosphate 5-phosphatase; src homology domain 2;

KW SH2 domain; signal transduction; Leukaemia; cancer; Grb2;

KV epidermal growth factor receptor binding protein.

XX Homo sapiens.

PN W09712039-A2.

PD 03-APR-1997.

XX 27-SEP-1996; 96WO-CA00655.

XX 14-JUN-1996; 96US-0664962.

PR 27-SEP-1995; 95US-0006063.

PR 30-NOV-1995; 95US-0007788.

PR 09-APR-1996; 96US-0015217.

XX (KRYG/) KRYSTAL G.

XX KRYSTAL G;

DR WPI; 1997-212898/19.

DR N-PSDB; AAT60302.

XX Inositol polyphosphate-5-phosphatase having SH2 domain - useful for

PT treating cancer and other conditions involving abnormal signalling

XX Disclosure; Page 47-48; 89pp; English.

XX Human epidermal growth factor receptor binding protein GRB2

CC (AAW14004) is an src homology domain 3 (SH3) protein that is capable

CC of binding to novel murine and human SHIP (SH2-containing inositol

CC phosphatase) proteins (see also AAW14002-03). It can be used in

CC methods for identifying agonists and antagonists of SHIP.

XX Sequence 217 AA;

Query Match 12.9%; Score 224; DB 16; Length 217;

Best Local Similarity 27.9%; Pred. No. 4e-12;

Matches 53; Conservative 44; Mismatches 57; Indels 36; Gaps 7;

```

QY 7 NFDSEERSWYGRSLRQDAVALLOGQRH-GVFLVRDSTSPGDVYLSVSENSRSHYIT 65
   | : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
   | : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
Db 51 nylemkhpwffgkikprakeemlskgrhdgafliresepdpdflsvkfgndvqhfv 110
   | : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
QY 66 NSSGPRPPVPPAPQPPVSPSRLRIGDQFDSLPALLEFYKIHVLDPTTLIEPVARSR 125
   | : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
Db 111 lrdg-----agkyflwvkvkfnslnelvqyhr-----sts-----vsrnq 144
   | : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
QY 126 QSGSVILRQ-----EEAEYRALFDFENGNDIEDLPFKKGILIRIDKPEQGMNAEDSEG 180
   | : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
Db 145 q---lftrdieqvppqplvqalfdldpqedgelfgrgdfihvmdnsdpnwkg-a-chg 200
   | : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
QY 181 KRGMIPVPV 190
   | : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
Db 201 qtgmfprrny 210

```

RESULT 10

AAW42070
ID AAW42070 standard; Protein; 217 AA.

AC AAW42070;

DT 04-JUN-1998 (first entry)

DE Growth factor receptor-bound protein 2.

XX Growth factor receptor-bound protein 2; Grb-2; CML; bcr-abl;

KM translation initiation site; chronic myelogenous leukaemia; cancer.

KW Homo sapiens.

OS Key Location/Qualifiers

FT Domain 5..54

FT Domain /label= SH3

FT Domain 60..158

FT Domain /label= SH2

FT Domain 163..208

FT Domain /label= SH3

PN W09801547-A1.

PD 15-JAN-1998.

XX 08-JUL-1997; 97WO-US10101.

XX 08-JUL-1996; 96US-0679437.

XX (TEXA) UNIV TEXAS SYSTEM.

XX Arlinghaus RB, Lopez-Berestein G, Tarr AM;

DR WPI; 1998-110229/10.

DR N-PSDB; AAV09213.

XX Use of anti-sense oligo:nucleotide(s) to Grb2 or Crkl nucleic acids

PT - for inhibiting growth of cancer cells in treatment of cancers,

XX particularly chronic myelogenous leukaemia

XX Disclosure; Fig 4; 47pp; English.

XX This is a polypeptide sequence of Grb-2. Translation of Grb-2 CDNA

CC can be inhibited by oligonucleotides of specific composition that

CC hybridise to its translation initiation site (see AAV09215).

CC The oligonucleotide compositions can be used for treating, particularly

CC chronic myelogenous leukaemia (CML).

XX Sequence 217 AA;

Query Match	12.9%	Score 224	DB 19	Length 217
Best Local Similarity	27.9%	Pred. No. 4e-12		
Matches	53	Conservative	44	Mismatches 57
				Indels 36
				Gaps 7

OY	7	NFDSESSRWYGRLSROEAVALLQGQRH-GVELVRDSSTSPGDVYLVSYSENSRVSHYII	65
		1 : : : : : 1 : : : : : 1 1 1 1 1 : : : : : 1 1 : : : :	
Db	51	nylemkhpwffgkprakeemlskqtrhdgaflreresapgdflskfgndvghfvc	110
OY	66	NSSGRPRPPPPADPPPEVSPSLRLRIGQDEDSLPALEFRKIKHYLDTTILLIPEVARSR	125
		1 :	
Db	111	lrdg-----agkyflwvkkfnslnelvdynr-----stc-----vsrvg	144
OY	126	QGSGLVLRQ-----EEAEYRALPFENGDEEDLFFPKKGIDILRIRKDPEDQWMAEDSEG	180
		1 :	
Db	145	q-----flldiegvpqprlyvgalfdldpdegedelgtrrgdfdhmndsqpnwkgc-chg	200
OY	181	KRGMTIPVPYV 190	
		: :	
Db	201	qlgmfprryv 210	

RESULT	11
ID	AAR84636
XX	AAR84636 standard; Protein; 217 AA.
AC	
XX	AAR84636;
DT	25-FEB-1996 (first entry)
XX	
DE	Grb2 protein.
XX	
KM	Grb2; BCR-ABL; tyrosine kinase; transformation; Ras; oncoprotein;
XX	leukaemia.
OS	Homo sapiens.
XX	
FH	Key
FT	Domain
FT	Domain
FT	Domain
FT	Domain
XX	
PB	CA2113494-A.
PD	15-JUL-1995.
XX	
PF	14-JAN-1994; 94CA-2113494.
XX	
PR	14-JAN-1994; 94CA-2113494.
XX	
PA	(MOUN) MOUNT SINAI HOSPITAL CORP.
PA	(TEXA) UNIV TEXAS.
XX	
PI	Arlinghaus R, Gish G, Liu J, Pawson A, Pull L;
XX	
DR	WPI: 1995-302931/40.
DR	N-PSDB; AAT05108.
XX	
PT	Detection of agents that modify BCR-ABL mediated transformation -
PT	useful in treatment of leukaemia and other malignancies
XX	
PS	Example 1; Page 48; 106pp; English.
XX	
CC	The human Grb2 protein (AAR84636) acts as an adaptor to link BCR-ABL
CC	tyrosine-kinase to mSosl (AA84638). The resulting BCR-ABL-Grb2-mSosl
CC	complex activates the Ras pathway leading to morphological
CC	transformation. Substances that affect this transformation are
CC	useful in the treatment of chronic, acute myelogenous or acute
CC	lymphocytic leukaemia, and are identified by reaction with
CC	Grb2 (or its SH2 or SH3 domains) and with a cpd. contg. the Grb2-
CC	binding site on BCR-ABL, Sos or Shc and examination of any resulting

[illegible]

RESULT	12	
AA026061		
ID	AA026061	standard; Protein; 317 AA.
XX		
AC	AA026061;	
XX		
DT	02-FEB-1993	(first entry)
XX		
DE	Growth Factor Receptor Bound protein GRB-2 partial sequence.	
XX		
KW	Tyrosine phosphorylation; epidermal growth factor receptor; EGFR.	
XX		
OS	Homo sapiens.	
XX		
PH	Key	Location/Qualifiers
FT	Domain	30
FT		/note= "start of SH2 domain"
FT	Domain	133
FT		/note= "start of SH3 domain"
FT	Misc-difference	183
FT		/note= "corresponds to CNG codon, where N is unknown"
FT	Misc-difference	184
FT		/note= "corresponds to TGA codon"
FT	Misc-difference	196
FT		/note= "corresponds to TAA codon"
FT	Misc-difference	199
FT		/note= "corresponds to TGA codon"
FT	Misc-difference	215
FT		/note= "corresponds to TGA codon"
FT	Misc-difference	231
FT		/note= "corresponds to TGA codon"
FT	Misc-difference	202
FT		/note= "corresponds to TAA codon"
FT	Misc-difference	299
FT		/note= "corresponds to TGA codon"
FT	Misc-difference	301
FT		/note= "corresponds to TAA codon"
FT	Misc-difference	302
FT		/note= "corresponds to TAA codon"
FT	Misc-difference	315
FT		/note= "corresponds to TAG codon"
XX		
PN	W09213001-A.	
XX		
PD	06-AUG-1992.	

PI Hansson V, Levy FO, Mustelin T, Skaltegg BS, Sundvold V, Tasken K;
 PI Vang T, Altman A, Munshi A;
 DR WPI: 2000-086801/07.
 DR N-PSDB: AA246490.
 XX
 PT Altering the activity of protein kinase signaling pathways, used for
 PT treating immunosuppressive disorders, e.g. AIDS, proliferative
 PT disorders, e.g. cancers or autoimmune diseases
 PS Claim 17; Page 93; 11pp; English.
 XX
 CC The invention provides a novel method of altering the activity of the
 CC protein kinase A (PKA) signaling pathway in a cell that comprises
 CC altering the extent of phosphorylation of one or more PKA substrates, or
 CC kinase substrates downstream in the PKA signaling pathway. Pharmaceutical
 CC compositions containing a nucleic acid molecule that encodes a PKA
 CC substrate, or fragment, precursor or functionally equivalent variant,
 CC where the sequence is modified to alter its susceptibility to
 CC phosphorylation by PKA can be used for treating a disorder exhibiting
 CC abnormal PKA signaling activity, immunosuppressive disorders or
 CC proliferative diseases. They can be used for treating e.g. HIV
 CC infection, AIDS, common variable immunodeficiency or cancers. Conditions
 CC in which upregulation of the PKA pathway is required, such as autoimmune
 CC disease, e.g. systemic lupus erythematosus, may also be treated. The
 CC present sequence represents a PKA substrate, wherein the substrate is in
 CC the Vav-family, preferably Vav, Vav2, Vav-3, Vav-3beta, Vav transforming
 CC protein and Vav-2 oncogene.
 XX
 SQ Sequence 845 AA;
 Query Match 10.0%; Score 174; DB 21; Length 845;
 Best Local Similarity 27.3%; Pred. No. 6.6e-07;
 Matches 54; Conservative 27; Mismatches 67; Indels 50; Gaps 8;
 QY 16 WYWGRLSROEAVALLQGRHGVFLVSDSTSPGDVLSVSENSRVSH-YIINSGPRPPV 74
 DB 671 WYAGPMERAGAESILANRSDGFTLVRYGVKDAAEFAISKYVKKHVKIMTAEG----- 725
 QY 75 PPSPAQPPPGVSPSRRLRGDOE-FDSLPALEFYK-----IHYLDYT----- 115
 DB 726 -----LYITLKKATFRGLTGLVEFYGNSLKDCFSIDTLTGFfKPEK 771
 QY 116 TLIEPVARSROGSGVILRQEAERYRALFDPNGNDEEDLPKKGDIIRIDKPEEQ-WMN 174
 DB 772 TLSPVAVSTKYfGT-----AKARYDfCARDSELSIKEGDILINKKYGQGW 822
 QY 175 AEDSEGRKMIPVYVER 192
 DB 823 GE-IYGRVGFANYVEE 839
 RESULT 15
 AAY27125
 ID AAY27125 standard; Protein; 797 AA.
 AC AAY27125;
 DT 14-SEP-1999 (first entry)
 DE Amino acid sequence of human Vav.
 XX
 KW LAT; tyrosine kinase; linker for activation of T cell; TCR; human;
 KW T-cell receptor; TCR signaling pathway; neoplasia; inflammation;
 KW hypersensitivity; allergy; microbial infection; genetic disease;
 KW autoimmune disease; graft rejection; modulator; Vav.
 OS Homo sapiens.
 XX
 PN MO9932627-A2.
 XX
 PD 01-JUL-1999.

XX
 PF 23-DEC-1998; 96WO-US27400.
 XX
 PR 23-DEC-1997; 97US-0068690.
 XX
 PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
 XX
 PI Samelson LE, Zhang W;
 XX
 DR WPI: 1999-418926/35.
 DR N-PSDB: AAX89078.
 XX
 PT Linker for activation of T cell protein used to, e.g. screen for
 PT modulators of T cell signalling
 PS Disclosure: Fig 11B; 125pp; English.
 XX
 CC The invention relates to a protein tyrosine kinase substrate LAT (linker
 CC for activation of T cells) protein. Modulation of interaction between LAT
 CC and the T-cell receptor (TCR) affects the TCR signalling pathway. LAT is
 CC a substrate for tyrosine kinases and becomes phosphorylated after TCR
 CC engagement, resulting in recruitment of other signalling molecules. LAT
 CC is used to identify and test (ant)agonists of tyrosine kinase signalling
 CC pathways, i.e. modulation of interaction between tyrosine kinase
 CC substrates and intracellular ligands or between these ligands and other
 CC members of the pathway, including identification of downstream signalling
 CC proteins, particularly in immune system cells. These modulators are
 CC potentially useful as drugs and diagnostic agents, particularly for
 CC diseases that involve undesirable cell proliferation, differentiation,
 CC growth or T cell anergy, e.g. neoplasia, inflammation, hypersensitivity/
 CC allergy, microbial infection, metabolic, genetic or autoimmune diseases,
 CC graft rejection. LAT is also used to generate specific antibodies, used
 CC for detection of LAT. Nucleic acid that encodes LAT, or its fragments,
 CC are used to identify homologous sequences in other species; to detect the
 CC LAT gene and as sources of antisense therapeutics. Modulators of LAT are
 CC potentially more specific and less toxic than known immunosuppressants
 CC such as cyclosporin. The present sequence represents the amino acid
 CC sequence of human Vav.
 XX
 SQ Sequence 797 AA;
 Query Match 10.0%; Score 172.5; DB 20; Length 797;
 Best Local Similarity 27.1%; Pred. No. 8.3e-07;
 Matches 54; Conservative 27; Mismatches 67; Indels 51; Gaps 8;
 QY 16 WYWGRLSROEAVALLQGRHGVFLVSDSTSPGDVLSVSENSRVSH-YIINSGPRPP 73
 DB 622 WYAGPMERAGAESILANRSDGFTLVRYGVKDAAEFAISKYVKKHVKIMTAEG----- 677
 QY 74 VPPSPAQPPPGVSPSRRLRGDOE-FDSLPALEFYK-----IHYLDYT----- 115
 DB 678 -----LYITLKKATFRGLTGLVEFYGNSLKDCFSIDTLTGFfKPEK 722
 QY 116 -TLIEPVARSROGSGVILRQEAERYRALFDPNGNDEEDLPKKGDIIRIDKPEEQ-WM 173
 DB 723 TLSPVAVSTKYfGT-----AKARYDfCARDSELSIKEGDILINKKYGQGW 773
 QY 174 NAEDEGRKMIPVYVER 192
 DB 774 RGE-IYGRVGFANYVEE 791

Search completed: September 27, 2001, 16:41:23
 Job time: 696 sec

